From Test Requisition to Result Interpretation: Challenges and Opportunities to Improve Molecular Genetic Testing

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Test Requisitions

Recommendations and Practices (DNA-based Cystic Fibrosis Testing)

Test requisitions serve to collect critical information necessary for reviewing the appropriateness of the test referral and interpretation of the test result. We identified 48 clinical laboratories offering DNA-based cystic fibrosis testing from the GeneTests database.[1] In a preliminary study, we collected 17 (35%) publicly available laboratory requisition forms and evaluated what information was requested. We report these observations together with requirements and recommendations put forward by the Clinical Laboratory Improvement Amendments, American College of Medical Genetics (ACMG), and NCCLS[2,3,4,5] The ACMG recommendations are further endorsed by a joint guideline prepared by both ACMG and the American College of Obstetricians and Gynecologists.[6]

References

1. GeneTests: Medical Genetics Information Resource (database online). Copyright, University of Washington and Children's Health System, Seattle. 1993-2003. Updated weekly. Available at http://www.genetests.org. Accessed March, 2003.
2. Health Care Financing Administration, US Department of Health and Human Services. Public Law 100-578.Code of Federal Regulations 2001;Part 493(Title 42):798-923.
3. Health Care Financing Administration. US Department of Health and Human Services (2003) Medicare, Medicaid, and CLIA Programs; Laboratory requirements relating to quality systems and certain personnel qualifications; final rule. Fed. Register 68:3640-3714.
4. American College of Medical Genetics, Copyright ACMG, 2002, Standards and guidelines for clinical genetics laboratories, Third Edition, 2003. Available at http://www.acmg.net/resources/s-g/s-g-yes-no.asp.
5. NCCLS. Molecular diagnostic methods for genetic diseases. Approved guidelines, NCCLS document MM1-A, volume 17. Wayne, PA: NCCLS Standards 2000.
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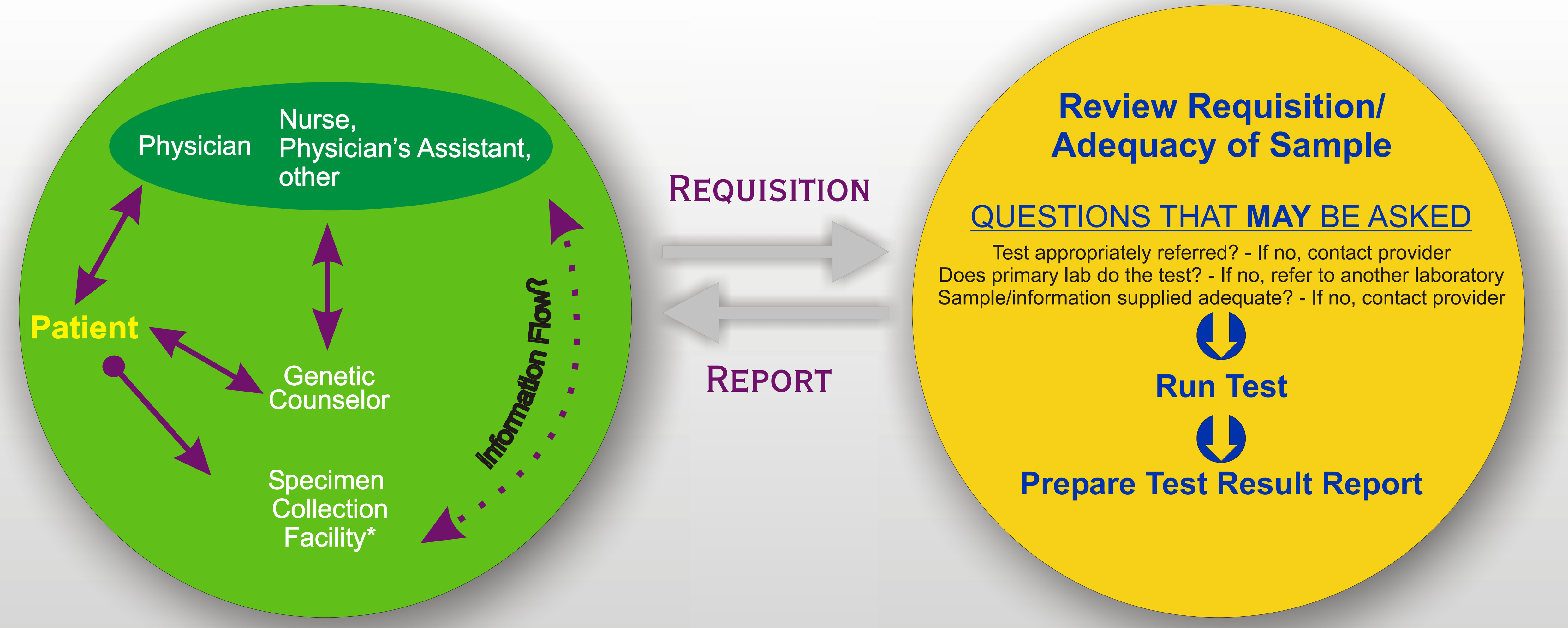
Content Summary of Cystic Fibrosis Requisition Forms Collected from US Laboratories

Information requested	Requisitions reviewed: Cystic fibrosis (% listed) (N=17)	CLIA required	ACMG recommended	NCCLS recommended
Physician's signature	18	authorized person ordering	+	+
Date of Birth	94	as relevant	+	+
Date of Sample Collection	76	+	as relevant	+
Sample Type	65	as relevant	as relevant	+
Indications for testing	88	as relevant	+	+
Patient clinical information	59	as relevant		as relevant
Family clinical information	41	as relevant	+	not specifically stated
Pedigree	47	as relevant	as relevant	+
Ethnicity	94	as relevant	+	+
Gender	82	as relevant	+	+
Pregnancy status	59	as relevant	as relevant	as relevant

Clinical Setting

Laboratory Setting



Test Reports

Recommendations and Practices (DNA-based Cystic Fibrosis and FV Leiden Testing)

The analytic result from a molecular genetic test often requires test specific, patient, family and population-based data to develop an interpretation most useful for clinical decision making. To determine to what extent laboratories offer such information on their test result report, a study was performed looking at actual reports collected from laboratories offering DNA-based cystic fibrosis and fV Leiden genetic testing.[7] At the time of this study, the GeneTests laboratory database listed 44 laboratories offering CF testing and 72 laboratories offering fV Leiden testing. Reports were collected from 28 (64%) of the CF laboratories and 46 (64%) from the fV laboratories. We evaluated the content of these reports and compared their content to requirements and recommendations of the Clinical Laboratory Improvement Amendments, American College of Medical Genetics (ACMG), and NCCLS.[2,3,4,5] The ACMG recommendations are endorsed by a joint guideline prepared by both ACMG and the American College of Obstetricians and Gynecologists.[6]

In a follow-up study, a cross-sectional survey was undertaken of US physicians from specialties likely to order CF or fV Leiden DNA-based genetic tests.[8] Physicians received one of three mock reports, of varying content complexity, and a one-page survey. The survey contained 22 Likert-type questions asking physicians to rate perceived usefulness of specific report elements on a scale ranging from 1 (poor) to 5 (excellent), with options for "not applicable" and "no information provided."

References

7. Andersson HC, Krousel-Wood MA, Jackson KE, Rice J, Lubin IM. 2002. Medical genetic test reporting for cystic fibrosis (ΔF508) and factor V Leiden in North American laboratories. Genetics in Medicine. 4:324-327.
8. Krousel-Wood MA, Andersson, HC, Rice R, Jackson KE, Rosner ER, Lubin IM. 2003. Physicians' perceived usefulness of and satisfaction with test reports for cystic fibrosis (ΔF508) and factor V Leiden, Genetics in Medicine, in press.

Content Summary of Cystic Fibrosis and Factor V Leiden Reports of those Collected from US and Canadian Laboratories

	Cystic Fibrosis (%) N=28	Factor V Leiden N=46 (%)	CLIA required	ACMG recommended	NCCLS recommended
Administrative elements					
Laboratory director signature	93	98	returned to authorized provider	+	+
Board certification listed	21	9	-		-
Specimen collection date	46	63	-	+	+
Specimen received date	68	80	-	+	+
Result date	96	98	+	+	+
Contact information	86	87	+	+	+
Patient-specific elements					
Clinical indications	64	39	-	+	+
Ethnicity listed	21	NA	-	+	+
Gender listed	46	46	-	-	-
DOB listed	79	80	-	-	+
Test-specific elements					
Interpretation	93	96	-	+	+
Methodology	64	80	as relevant	+	+
Mutations listed	96	NA	as relevant	+	+
Detection rate	86	NA	as relevant	as relevant	+
Post-specific elements					
Adjusted risk	71	NA	as relevant		+
Genetic counseling	61	52	-	+	+

Physician Perceived Usefulness for Report Content

Cystic fibrosis physician perceived usefulness for report components

	Mock report A: most comprehensive mean +/- SD (n)	Mock report B: intermediate mean +/- SD (n)	Mock report C: least comprehensive mean +/- SD (n)	P value	Newman Keuls	Correlation with satisfaction
What test performed	4.34 +/- 0.81 (44)	4.16 +/- 0.99 (56)	3.13 +/- 1.59 (39)	<0.0001	A,B>C	0.66a
Test Methodology	4.13 +/- 0.87 (45)	3.98 +/- 1.00 (56)	2.05 +/- 1.34 (40)	<0.0001	A,B>C	0.62a
Test limitation	3.91 +/- 1.06 (45)	3.19 +/- 1.32 (54)	2.35 +/- 1.39 (40)	<0.0001	A>B>C	0.63a
Test Result	4.18 +/- 0.89 (45)	3.93 +/- 1.04 (54)	3.15 +/- 1.17 (41)	<0.0001	A,B>C	0.71a
Test report format	3.62 +/- 094 (45)	3.62 +/- 1.13 (55)	3.13 +/- 1.32 (40)	0.12	NA	0.67a
Clinical history	3.31 +/- 1.16 (45)	2.75 +/- 1.41 (51)	2.28 +/- 1.37 (36)	0.0013	A>B,C	0.59a
Linkage: ethnicity and mutation panel	3.89 +/- 1.09 (45)	1.88 +/- 1.24 (51)	1.71 +/- 1.14 (38)	<0.0001	A>B,C	0.58a
Clinical decision making	3.59 +/- 1.09 (44)	3.25 +/- 1.17 (55)	2.36 +/- 1.32 (42)	<0.0001	A,B>C	0.77a
Recommendations regarding follow-up testing	3.24 +/- 1.09 (41)	2.75 +/- 1.25 (53)	1.73 +/- 1.18 (41)	<0.0001	A,B>C	0.60a
Genetic counseling	3.70 +/- 0.88 (44)	3.64 +/- 1.08 (55)	1.83 +/- 1.38 (42)	<0.0001	A,B>C	0.74a
Clinical Implications for other family members	3.42 +/- 1.07 (43)	3.49 +/- 1.27 (55)	1.83 +/- 1.30 (41)	<0.0001	A,B>C	0.72a
Contact information	3.80 +/- 1.17 (44)	3.55 +/- 1.25 (56)	3.48 +/- 1.35 (42)	0.39	NA	0.40a

SD, standard deviation
1=poor; 5=excellent
aP<0.001

Factor V Leiden physician perceived usefulness for report components

	Mock report D: most comprehensive mean +/- SD (n)	Mock report E: intermediate mean +/- SD (n)	Mock report F: least comprehensive mean +/- SD (n)	P value	Newman Keuls	Correlation with satisfaction
What test performed	[illegible]	[illegible]	[illegible]	[illegible]	D,E>F	[illegible]
Test Methodology	[illegible]	[illegible]	[illegible]	<0.0001	D,E>F	[illegible]
Test limitation	[illegible]	[illegible]	[illegible]	[illegible]	NA	[illegible]
Test Result	[illegible]	[illegible]	[illegible]	[illegible]	D,E>F	[illegible]
Test report format	[illegible]	[illegible]	[illegible]	[illegible]	D,E>F	[illegible]
Clinical history	[illegible]	[illegible]	[illegible]	[illegible]	D>E,F	[illegible]
Clinical decision making	[illegible]	[illegible]	[illegible]	[illegible]	D,E>F	[illegible]
Recommendations regarding follow-up testing	[illegible]	[illegible]	[illegible]	<0.0001	D,E>F	[illegible]
Genetic counseling	[illegible]	[illegible]	[illegible]	<0.0001	D,E>F	[illegible]
Clinical Implications for other family members	[illegible]	[illegible]	[illegible]	<0.0001	D,E>F	[illegible]
Contact information	[illegible]	[illegible]	[illegible]	[illegible]	D,E>F	[illegible]

SD, standard deviation
1=poor; 5=excellent
aP<0.001

Introduction

In this study, we sought to assess and compare regulatory and voluntary guidance for molecular genetic test requisitions and test result reports to actual practices. We looked at cystic fibrosis and fV Leiden testing requisitions and result reports as models. Molecular genetic tests do not directly measure a physiologic or pathologic condition. As such, results from such tests generally only have meaning when considered in light of other patient, family, and test specific information. Even when such information is available, variable expression and penetrance of the genotype can make interpretation difficult. We observed far more attention has been accorded by regulatory and professional groups in defining the content of test result reports than what should be part of the test requisition process. In practice, significant variability for both the requisition form and test result report was observed. This suggests that many laboratories are either not collecting or using important information needed to prepare an appropriate test result report. Results from a physicians' survey indicated participants desired a report sufficiently comprehensive to be of value in clinical decision-making. These observations suggest a need for improving the collection and use of critical information necessary to assure genetic tests and results are being appropriately referred and interpreted. Opportunities for improving practices may take the form of educational activities, resource development, and guidance from professional organizations. To address these issues, in part, a conference/workshop is being planned that will bring together clinical practitioners, laboratorians, private and governmental groups, and others to begin the process by which these issues can be considered and resolved.

Summary

1. The collection and use of patient and family information are critical for properly interpreting the genetic test result.
2. Multiple professionals, not always in close contact with each other or with the patient, can each have a role in developing the test requisition and using the test result report.
3. Current regulatory and voluntary guidelines provide detailed guidance for test result report content but fail to provide equivalent attention to the requisition process.
4. Within our limited assessment of available requisition forms for DNA-based cystic fibrosis testing, variability in both content and format was observed.
5. In several cases, requisition forms requested less information than necessary to comply with recommendations from voluntary guidelines.
6. Variability existed in report content among North American laboratories performing CF and fV Leiden testing.
7. Information which may affect the physician's management of the patient (e.g., test methodology, post-test adjusted risk for being a mutation carrier, consideration of genetic counseling) is not uniformly included in CF and fV Leiden test reports.
8. A physicians' survey revealed greater perceived usefulness:
   1) with more comprehensive test result reports
   2) for the inclusion of information about genetic counseling
   3) for additional information regarding the clinical implication of the test result for other family members

Challenges and Opportunities for Improving Molecular Genetic Testing

1. Those drafting voluntary guidelines should more carefully consider the requisition process and practical measures to ensure the collection and use of appropriate patient and family information.
2. No uniform formats are used for collecting particular information such as ethnicity, family history and pedigree. Guidance for the collection of such information should be considered.
3. Genetic test result reports serve to provide key information to the clinical practitioner in making patient management decisions. Such reports may be reviewed and used by a number of clinical practitioners, some of whom may not be privy to the original referral. Therefore, the report should be sufficiently complete and understandable by all parties whom may use it.
4. In one effort to address this need, a conference/workshop has been developed to bring together physicians, nurses, laboratorians, genetic counselors, public health professionals, and others to explore opportunities for improving the genetic testing process.

Conference/Workshop Announcement

COMMUNICATION: Key to Appropriate Genetic Test Referral, Result Reporting and Interpretation

Meeting Objectives:

- Explore the changing roles of professionals in the use of genetic tests for clinical and public health practice using cystic fibrosis DNA-based testing as a model for discussion.
- Explore the challenge of communication among the varied professionals involved in the referral, reporting, and interpretation of genetic tests and results.
- Develop ideas for improving the communication of key information necessary for assuring genetic tests are appropriately referred and the results correctly interpreted.

Format:
Short talks , a panel discussion, and workgroups will provide opportunities for candid discussions about existing practices and challenges inherent in the offering of genetic testing services in a variety of practice settings.

Participants:
Physicians, nurses, genetic counselors, laboratorians, public health professionals, policy makers, patient advocates, payers and representatives from professional and trade organizations.

Hosting/Date/Location:
This conference/workshop is being hosted by Mt. Sinai School of Medicine and the Centers for Disease Control and Prevention. This event will be held May 2-3, 2003 at Mt. Sinai School of Medicine.

Interested in participating or learning more:
Participation is primarily by invitation but additional limited space is available for others who wish to attend. For additional information or if you wish to attend, please contact:

Dr. Peggy McGovern at (212) 241-9234 or mmcgovern@mssm.edu
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